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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/578,212
Filing Date: May 04, 2006
Appellant(s): WELTER ET AL.

Richard Sutkus
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 16 May 2011 appealing from the Office action mailed 14 July 2010.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application:

Claims 1-14 and 42-44 are rejected.

Claims 15-41 are withdrawn.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the

subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

WO 02/06441	Vetillard et al	24 January 2002
US 2004/0132175	Vetillard et al	08 July 2004
US 2004/0077075	Jensen et al	22 April 2004

Vetillard '441 is directed to a bioreactor comprising a cell culture chamber bound by a plurality of gas permeable membranes, wherein critical culture components are added to and removed from the chamber using a loading module capable of transmitting a hydrostatic pressure through at least one membrane.

Vetillard '175 is an English language equivalent of Vetillard '441.

Jensen is directed to a bioreactor that transmits critical culture components through a membrane using a hydrostatic pressure, or, alternatively, a variety of different functionally equivalent forces.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1) Claims 1-9, 12, 14, 43 and 44 are rejected under 35 U.S.C. 102(b) as being anticipated by Vetillard (WO 0206441) – see English language (US 20040132175) for a translation.

With respect to claims 1 and 43, Vetillard discloses a bioreactor comprising a housing (Figure 1:C2) defining a first chamber that contains a first liquid medium. The housing comprises an inlet port (Figure 1:EF2) and an outlet port (Figure 1:SF2) to accommodate a culture medium fluid flow through the first chamber. This is disclosed in paragraphs [0080] and [0096] of US 20040132175. Gas permeable membranes (Figure 1:M1 and Figure 1:M3) define a portion of the housing and allow gas to flow through the housing into the first chamber. Loading modules (Figure 1:C1 and Figure 1:C3) are fully capable of transmitting hydrostatic pressure through the membranes to the first liquid medium contained in the first chamber. Paragraphs [0109], [0134] and [0140]-[0146] indicate that a "downward phase" and an "ascending phase" are created by varying pressures within the loading modules. Furthermore, Vetillard expressly discloses that each inlet and outlet is in communication with at least one pump and valve that are capable of regulating when fluid is added and removed from a

corresponding chamber. This is described in paragraphs [0109], [0115] and [0117], and is shown in Figure 6

With respect to claim 2, Vetillard discloses the apparatus in claim 1 wherein the hydrostatic loading module is capable of transmitting pressure by a static second liquid medium. Although Vetillard does not expressly indicate that fluid is retained at a static state within the loading modules before release through the outlet, the device of Vetillard is fully capable of being operated according to this intended use.

With respect to claims 3, 9 and 44, Vetillard discloses the apparatus in claim 1 wherein the hydrostatic modules are attached to the housing and form second and third chambers with the housing. The second and third chambers are separated from the first chamber by gas permeable membranes. This is depicted in Figure 1.

With respect to claims 4 and 5, Vetillard discloses the apparatus in claim 3 wherein the hydrostatic loading modules include pumps (Figure 6:P1 and Figure 6:P3) for increasing and decreasing the pressure of each loading module.

With respect to claim 6, Vetillard discloses the apparatus in claim 4 wherein each loading module comprises an electronic pressure gauge for monitoring pressure in each chamber. This is described in paragraph [0144].

With respect to claims 7 and 8, Vetillard discloses the apparatus in claim 1 wherein the housing comprises a frame that includes a first surface spaced apart from a second surface. The walls of the housing depicted in Figure 1 are considered to represent first and second surfaces. The fluid inlet and fluid outlet are considered to be openings that extend through the frame.

With respect to claim 12, Vetillard discloses the apparatus in claim 1 wherein a pH sensor is provided. This is disclosed in paragraph [0106].

With respect to claim 14, Vetillard discloses the apparatus in claim 1 wherein control valves (Figure 6:V2E1-V2E3, V2S1-V2S3) and pumps are provided for regulating fluid flow through inlets and outlets. This is described in paragraphs [0109], [0115] and [0117], and is shown in Figure 6.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2) Claims 1-14 and 42-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vetillard (WO 0206441) as applied to claim 1, and further in view of Jensen (US 20040077075).

With respect to claims 1-9, 12, 14, 43 and 44, Vetillard discloses the apparatus as previously described above. For the sake of argument and in order to expedite prosecution, if Vetillard does not disclose transmitting a hydrostatic pressure and if limitations drawn to the transmission of a hydrostatic pressure do not represent an intended use, then Vetillard fails to anticipate the claims.

Jensen discloses a micro bioreactor comprising a cell culture chamber bound by two membranes capable of allowing the perfusion of gases, nutrients and water. This is disclosed in Figure 2A and paragraphs [0067]-[0074]. Jensen further teaches in paragraphs [0190] and [0194] that diffusion through the membranes is produced through the transmission of hydrostatic pressure.

Vetillard and Jensen are analogous art because they are from the same field of endeavor regarding bioreactors comprising gas permeable membranes.

At the time of the invention, it would have been obvious to ensure that the Vetillard apparatus allows for the transmission of a hydrostatic pressure capable of

promoting diffusion of desired compounds through the membranes. As evidenced by Jensen, hydrostatic pressure within the culture and fluid chambers can be precisely controlled in order to promote appropriate culture conditions. One of ordinary skill would have recognized that only minor (if any) structural alterations would be necessary to generate a hydrostatic pressure within the apparatus of Vetillard.

With respect to claim 10, Vetillard discloses the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 102 rejections above, however does not expressly indicate that the membrane is optically transparent.

Jensen discloses a bioreactor comprising a plurality of chambers divided by a plurality of membranes (see Figure 2A). Jensen teaches that the gas permeable membranes are constructed from optically transparent materials. This is described throughout the reference and is presented in claim 19.

Vetillard and Jensen are analogous art because they are from the same field of endeavor regarding bioreactors comprising gas permeable membranes.

At the time of the invention, it would have been obvious to ensure that the membranes disclosed by Vetillard are constructed from optically transparent materials. Jensen teaches that this is beneficial because it allows one to better detect cell growth and metabolism using sensors that rely on bioluminescence. As evidenced by Jensen, biocompatible optically transparent membrane materials are readily available in the art.

With respect to claim 11, Vetillard and Jensen disclose the apparatus set forth in claim 10 as set forth in the 35 U.S.C. 103 rejection above. In addition, Jensen teaches in paragraph [0103] that the interior surfaces of the bioreactor are coated with a material resistant to cell attachment. Claims 28 and 29 further disclose the use of a substance that decreases adsorption of cells.

At the time of the invention, it would have been obvious to ensure that the gas permeable membrane disclosed by Vetillard was coated by a material resistant to cell attachment. One of ordinary skill in the art would have found it desirable to prevent attachment of cells to the Vetillard membrane in order to avoid clogging of the membrane pores. As evidenced by Jensen, coatings that decrease adsorption of cells to a surface are known in the art.

With respect to claim 13, Vetillard discloses the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 102 rejection above. In addition, Jenson states in paragraphs [0161] and [0176] that magnetic stir bars are used to agitate the cell solution during fermentation.

At the time of the invention, it would have been obvious to use the magnetic impellers disclosed by Jensen in the first liquid medium chamber disclosed by Vetillard. Jensen teaches that magnetic stir bars are well known in the art, simple in operation, and effective in agitating and aerating a solution.

With respect to claim 42, Vetillard discloses the apparatus set forth in claim 1, however does not expressly state that the gas permeable membranes are identical.

Jensen discloses the apparatus as previously described above. Jensen additionally teaches in paragraph [0064] that the first and second membranes formed on either side of the culture chamber may be made from the same materials having the same gas diffusivity and solubility properties.

At the time of the invention, it would have been obvious to ensure that the Vetillard membranes were identical. Jensen indicates in paragraph [0064] that it is known in the art to provide membrane pairs that are either identical or different depending on the requirements of the particular cell culture system at hand. More specifically, Jensen indicates that it is known to construct membranes that are specific to the type of culture medium space and/or gas space with which they interact. Accordingly, one of ordinary skill in the art would have recognized that it would have been beneficial to ensure that the Vetillard membranes were identical if both of the membranes interact with the same type of culture fluid or are intended to perform the same function.

(10) Response to Argument

Claims 1-9, 12, 14, 43 and 44 are rejected under 35 U.S.C. 102(b) as being anticipated by Vetillard (WO 0206441) – see English language (US 20040132175) for a translation.

Appellant's principle arguments are

(a) In the present case, claim 1 positively recites a hydrostatic – not hydrodynamic – loading module. The claim actually requires a hydrostatic loading module that actually transmits hydrostatic pressure through a membrane. The recitation that the hydrostatic loading module transmits hydrostatic pressure is a functional recitation and not a statement of intended use.

In response, please consider the following remarks.

Most, if not all, intended use recitations are functional limitations in that they describe how a positively recited element is operated. A limitation does not cease to be an intended use recitation simple because it is deemed to be "functional." While intended use recitations and other types of functional language cannot be entirely disregarded, in apparatus claims intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. *In re Casey*, 370 F.2d 576 (CCPA 1967); *In re Otto*, 312 F.2d 937 (CCPA 1963). Claims directed to apparatus must be distinguished from the prior art in terms of structure rather than function. *In re Danly*, 263 F.2d 844 (CCPA 1959). See also MPEP 2114. The manner of operating the device does not differentiate an apparatus claim from the prior art. A claim containing a "recitation with respect to the manner in which a claimed apparatus is intended to be employed does not differentiate the claimed apparatus from a prior art apparatus" if the prior art apparatus teaches all the structural limitation of the claim. *Ex parte Masham*, 2 USPQ 2d 1647 (BPAI 1987).

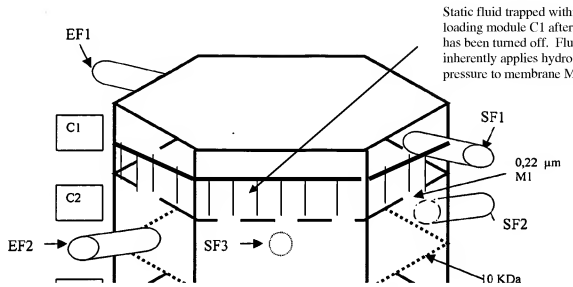
The instant case is very similar to *In re Schreiber* (*In re Schreiber*, 128 F.3d 1473 (Fed. Cir. 1997)) in which a prior art dispensing cap anticipated the applicant's claim because the cap was determined to be inherently capable of delivering popcorn, even though the prior art device was actually designed for dispensing oil. With respect to the present case, the Vetillard apparatus is inherently capable of imparting a hydrostatic pressure on cell culture chamber by sealing the fluid chambers surrounding the cell culture chamber by controlling when fluid is added and withdrawn.

(b) Vetillard requires hydrodynamic conditions. For example, the nutritive media F1 is not fluidly isolated or otherwise held static within the zone C1 at any time. This is because neither of the zones C1, C3 is capable of being sealed with liquid media F1, F3 therein in order to hydrostatically load the zone C2. There are no valves on either the fluid intake or output side of the zone C1 that would allow the zone to be sealed with liquid media F1 therein.

In response, please consider the following remarks.

Valves are not required to fill Vetillard's zone C1 with a fluid in order to apply a hydrostatic pressure to cell culture zone C2 across the membrane. Rather, hydrostatic loading would readily be accomplished simply by activating pump P1 and filling zone C1 with fluid from the expansion vessel. When zone C1 is full, pump P1 would merely be turned off, and fluid delivered to C1 would remain static while naturally imparting a hydrostatic force to the neighboring membrane. There is simply no teaching in Vetillard that would suggest that fluid added to the loading modules necessarily must drain out of

the module due to the lack of an outlet valve. In fact, it could not, as a result of the positioning of Vetillard's inlet and outlet tubes:



Importantly, it is additionally noted that nowhere in Appellant's written description, Figures, or claims are valves or other sealing means used to trap fluid within the first and second loading modules ever described or depicted. Appellant cannot argue that the Vetillard loading modules are incapable of transmitting a hydrostatic pressure because they are not in communication with inlet and outlets valves when Appellant's own invention does not rely on these features to generate hydrostatic forces. For example, there are no valves or other sealing mechanisms within lines 150, 154, 160, 164 (see Figure 2) that are used to statically isolate fluid within the loading modules. Because there is absolutely no structural difference between Appellant's claimed invention and that of Vetillard, Vetillard must be capable of fulfilling the intended use (i.e. hydrostatic loading) set forth in the clams.

(c) With respect to claim 43, Vetillard does not disclose that the inlet port to and the outlet port from the cell culture chamber are sealed. There is no indication that module C2 can be sealed during operation.

In response, please consider the following remarks.

Vetillard expressly discloses that the cell culture module C2 is in communication with inlet and outlet ports that are regulated by valves configured to seal the cell culture module. Vales V2E1-V2E3 (see Figure 6) may be closed to seal module C2 from the inlet side. Valves V2S1-V2S3 may be closed to seal the module C2 from the outlet side. All valves may be closed to completely seal cell culture module C2 during any time, including during hydrostatic loading.

(d) With respect to claim 44, Vetillard does not disclose that the Vetillard second chamber is sealed.

In response, please consider the following remarks.

Both of Vetillard's loading modules are sealed to the membranes of the cell culture chamber to prevent external contamination and leakage from the bioreactor. By tightly connecting the loading modules to the cell culture module, hydrostatic pressure may successfully be transmitted from each loading module through a membrane and to the cell culture module.

Claims 1-14 and 42-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vetillard (WO 0206441) as applied to claim 1, and further in view of Jensen (US 20040077075).

Appellant's principle arguments are

(a) The Vetillard apparatus is configured for bi-directional flow. Vetillard discloses a specific bioreactor shape and construction to ensure the efficacy of a hydrodynamically loaded bioreactor. One of ordinary skill would not have operated the Vetillard bioreactor under hydrostatic conditions because the system includes features designed to enhance cell growth under bi-directional dynamic flow conditions.

In response, please consider the following remarks.

Appellant does not allege that the system of Vetillard is incapable of being used to apply hydrostatic pressures through the membranes, or that the fundamental mode of operation (i.e. the exchange of nutrients, gases and wastes through the membranes) would be frustrated by using hydrostatic loading. All parties seem to agree that there is no "teaching away" issue. "A reference does not teach away if it merely expresses a general preference for an alternative invention, but does not 'criticize, discredit, or otherwise discourage' investigation into the invention claimed." *DeDuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 567 F.3d 1314, 1327 (Fed. Cir. 2009) (quoting *In re Fulton*, 391 F.3d 1195, 1201 (Fed. Cir. 2004).

Rather, Appellant states that one would not be motivated to pursue hydrostatic loading when the Vetillard bioreactor includes features (i.e. chamber shape & inlet/outlet placement) that allow it to be used under hydrodynamic conditions. As evidenced by

Jensen, however, it is well known in the art that hydrostatic loading may be used to deliver nutrients and other critical culture components across a porous membrane in a controlled manner. When considering exactly how to operate the bioreactor of Vetillard, it is entirely within the purview of one of ordinary skill to look to "identified, predictable solutions" and "pursue known options within his or her technical grasp." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 409 (2007). Jensen makes it clear that hydrostatic loading is a well known, functionally equivalent substitute for nutrient perfusion via dynamic, bi-directional flow. Because Jensen teaches that hydrostatic pressure may be used to predictably and successfully delivery key gases and metabolites across a membrane, one of ordinary skill would have expected the Vetillard system to operate in the same conventional and capable manner when hydrostatic loading is substituted for continuous bi-directional flow. While it is true that the location of the inlet and outlet couples and inner wall configurations disclosed by Vetillard are specifically designed to enable hydrodynamic conditions, they in no way would retard cell growth should the Vetillard system be operated under hydrostatic conditions. Simply because the Vetillard apparatus was designed with hydrodynamic flow conditions in mind does not mean that one of ordinary skill would be unable to achieve a similar result via hydrostatic loading.

(b) With respect to claim 42, Vetillard specifically discloses that membranes M1 and M3 are configured to have different cutting thresholds with respect to the perfusion of solid cell wastes and growth factors.

In response, please consider the following remarks.

Vetillard never requires that membranes M1 and M3 should or must be characterized by different gas permeability. While it is agreed that the membranes of the Vetillard apparatus are disclosed as having different cutting thresholds (i.e. pore sizes), Vetillard teaches that this serves to allow the selective diffusion of relatively large molecules such as nutrients, proteins and wastes. There is no evidence that membranes M1 and M3 of Vetillard are characterized by different permeabilities with respect to gases, especially since the gas permeability of any given membrane has just as much to do with material and thickness as it does pore size.

Furthermore, one of ordinary skill would have found it obvious to alter and experiment with the particular pore sizes disclosed by Vetillard. Jensen specifically indicates in paragraph [0064] that it is known in the art to provide membrane pairs that are either identical or different depending on the requirements of the particular cell culture system at hand. It is well known that various cell cultures have different requirements and purposes. For example, in bioreactors where nutrient delivery is paramount, one of ordinary skill would have found it obvious to diffuse nutrients through both membranes of the Vetillard apparatus. The fundamental mode of operation disclosed by Vetillard – the delivery and withdrawal of certain particulates to and from the cell culture – could readily be accomplished using a wide variety of membrane combinations.

(c) With respect to claim 43, Vetillard does not disclose that the inlet port to and the outlet port from the cell culture chamber are sealed. There is no indication that module C2 can be sealed during operation.

In response, please consider the following remarks.

Vetillard expressly discloses that the cell culture module C2 is in communication with inlet and outlet ports that are regulated by valves configured to seal the cell culture module. Vales V2E1-V2E3 (see Figure 6) may be closed to seal module C2 from the inlet side. Valves V2S1-V2S3 may be closed to seal the module C2 from the outlet side. All valves may be closed to completely seal cell culture module C2 during any time, including during hydrostatic loading.

(d) With respect to claim 44, Vetillard does not disclose that the Vetillard second chamber is sealed.

In response, please consider the following remarks.

Both of Vetillard's loading modules are sealed to the membranes of the cell culture chamber to prevent external contamination and leakage from the bioreactor. By tightly connecting the loading modules to the cell culture module, hydrostatic pressure may successfully be transmitted from each loading module through a membrane and to the cell culture module.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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